PTC/SS/65 (11-95)

Approved for use grouph 10/31/29. ONS 0551-0031

Patient and Tracement Office: U.S. DEPARTMENT OF COMMERCE

Patient and Tracement Union (choose a veid ONS control number.)

A STATE OF THE PROPERTY OF THE	Peters and Trademan Course & discurse a weld ONE control rustice.
REQUEST FOR ACCESS OF ABANG	DONED APPLICATION UNDER 37 CFR 1.14(a)
110000	In re Application of
	Application Number Filed
·•	08/332 646 11-1-94
-	Group An Una Erzminer
	Paper No.
· · · · · · · · · · · · · · · · · · ·	
Assistant Commissioner for Patents Washington, OC 20231	
(A) referred to in United States Patent No. (B) referred to in an application that is of Application No. paper number	note to public inspection as set form in 37 CFR 1.11, Le., on page of filed on page of filed or filed an authorization to lay open the complete or filed
Signature Typed or printed name	FOR FTO USE ONLY Approved by: (Initials)
	Thours to complete. The will vary copenaing upon the needs of the matrice of the
This form is esumated to take 0.4	An in complete 173 17 3-45 FORMS TO THIS ADDRESS. DELIG







(12) United States Patent

Winter et al.

(10) Patent No.:

US 6,248,516 B1

(45) Date of Patent:

Jun. 19, 2001

(54) SINGLE DOMAIN LIGANDS, RECEPTORS COMPRISING SAID LIGANDS METHODS FOR THEIR PRODUCTION, AND USE OF SAID LIGANDS AND RECEPTORS

(75) Inventors: Gregory Paul Winter; Elizabeth Sally Ward, both of Cambridge; Detlef Güssow, Abington, all of (GB)

(73) Assignee: Medical Research Council, London (GB)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: 08/470,031

(22) Filed: Jun. 6, 1995

Mar. 16, 1989

Related U.S. Application Data

(62) Division of application No. 08/332,046, filed on Nov. 1, 1994, which is a continuation of application No. 07/796,805, filed on Nov. 25, 1991, which is a division of application No. 07/580,374, filed on Sep. 11, 1990, now abandoned.

(GB) 8826444

(GB) 8906034

23.4, 23.5, 23.6

(30) Foreign Application Priority Data

Apr.	22, 1989	(GB)	8909217
May	15, 1989	(GB)	8911047
Jur	1. 2, 1989	(GB)	8912652
Jun.	16, 1989	(GB)	8913900
Aug.	15, 1989	(GB)	8918543
Nov.	13, 1989	(WÓ)	PCT/GB89/01344
(51)	Int. Cl.7		C12Q 1/68
(52)	U.S. Cl.	435/6	6; 435/69.6; 435/252.33;
. ,			435/441; 435/446
(58)	17t1.1	Sourch	435/240.2, 252.3,
(20)	rieia or	JUANUA	·········· T.J.J/ 4.T(J.4., 4.J.4.J.,
(30)	rieid of		9.6, 441, 446; 536/23.7,

(56) References Cited

U.S. PATENT DOCUMENTS

4,356,270	10/1982	Itakura .
4,642,334	2/1987	Moore et al
4,656,134	4/1987	Ringold .
4,683,195	7/1987	Mullis et al
4,683,202	7/1987	Mullis .
4,704,692	11/1987	Ladner.
4,711,845	12/1987	Gelfand et al
4,714,681	12/1987	Reading .
4,800,159	1/1989	Mullis et al
4,806,471	2/1989	Molin et al
4,816,397	3/1989	Boss et al
4,889,818	12/1989	Gelfand et al
4,937,193	6/1990	Hinchliffe et al.
4,946,786	8/1990	Tabor et al
4,959,317	9/1990	Sauer.

4,965,188	10/1990	Mullis et al
4,978,743	12/1990	Selbeck et al
4,983,728	1/1991	Herzog et al
5,023,171	6/1991	Ho et al

(List continued on next page.)

FOREIGN PATENT DOCUMENTS

2016841		11/1990	(CA).
2019323		12/1990	(CA).
0 120 694		10/1984	(EP)
0 125 023		11/1984	ÈΡ).
0 171 496		2/1986	(EP).
0 173 494		3/1986	(ΈP).
0 194 276 B1		9/1986	(EP).
0 200 362		12/1986	(EP) .
0 201 184 B1		12/1986	(ΈP).
0 239 400		9/1987	(EP).
0 368 684		5/1990	(EP) .
2 137 631		10/1984	(GB).
61-104788		5/1986	(JP) ́.
63-152984		6/1988	(JP) .
WO 86/01533		3/1986	(wo).
WO 87/02671	٠	5/1987	(wo).
WO-A			` ′
88/01649		3/1988	(WO).
WO 88/ 0663		9/1988	(wo).
WO 88/06630		9/1988	(wo).
WO 88/09344		12/1988	(wo).
WO 89/00999		2/1989	(wo).
WO 90/14424		11/1990	(wo).
WO 90/14430		11/1990	(wo).
WO 90/14443		11/1990	(wo).
WO-A			,
97/08320		3/1997	(WO).
			- /

OTHER PUBLICATIONS

Kokubu, F., et al, *The EMBO Journal*, vol. 7, No. 7, pp. 1979–1988, 1988 "Complete structure and organization of immunoglobulin heavy chain constant region genes in a phylogenetically primitive vertebrate".

Schwager, J., et al, *Proc. Natl. Acad. Sci. USA*, vol. 85, pp. 2245–2249, Apr. 1988 Immunology "Amino acid sequence of heavy chain from *Xenopus laevis* IgM deduced from cDNA sequence: Implications for evolution of immunoglobulin domains".

Roth, M.E., et al, *Science*, vol. 241, pp. 1354–1358, Sep. 9, 1988 "Selection of Variable–Joining Region Combinations in the α Chain of the T Cell Receptor".

(List continued on next page.)

Primary Examiner—James Ketter (74) Attorney, Agent, or Firm—Nixon & Vanderhye PC

(57) ABSTRACT

The present invention relates to single domain ligands derived from molecules in the immunoglobulin (Ig) superfamily, receptors comprising at least one such ligand, methods for cloning, amplifying and expressing DNA sequences encoding such ligands, preferably using the polymerase chain reaction, methods for the use of said DNA sequences in the production of Ig-type molecules and said ligands or receptors, and the use of said ligands or receptors in therapy, diagnosis and catalysis.

21 Claims, 23 Drawing Sheets